



## UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/929,985	08/14/2001	James K. Mainquist	P1013US10	3858
29490 7590 12/02/2008 GENOMICS INSTITUTE OF THE NOVARTIS RESEARCH FOUNDATION 10675 JOHN JAY HOPKINS DRIVE, SUITE E225 SAN DIEGO, CA 92121-1127				
EXAMINER				
SODERQUIST, ARLEN				
ART UNIT		PAPER NUMBER		
1797				
NOTIFICATION DATE		DELIVERY MODE		
12/02/2008		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPLegal@gnf.org

jclarke@gnf.org

ssesnovich@gnf.org

# Office Action Summary

Application No.

09/929,985

Applicant(s)

MAINQUIST ET AL.

Examiner

Arlen Soderquist

Art Unit

1797

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 07 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-15, 17-24, 27, 28, 35 and 37-42 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 14, 15 and 17-20 is/are allowed.
- 6) ☒ Claim(s) 1-13, 21-24, 27, 28, 35 and 37-42 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 January 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-302)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 7, 2008 has been entered.
2. The drawings were received on January 2, 2008. These drawings are acceptable.
3. Based on the specification and applicant's arguments relative to the 112 second paragraph rejection (starting at page 13 of the response dated 1-2-08) examiner, for examining purposes, is treating the inner and outer wall terms as found in the claims as follows. The term "outer wall" will be treated by examiner as a wall that defines the perimeter or peripheral shape of the microtiter plate and any structure connecting it to the walls and/or structure which defines the wells of the microtiter plate. An inner wall for examining purposes is as any wall or structure that defines the wells of the microtiter plate (paragraphs 13 and 19). Thus, relative to the claims that require alignment members, examiner will treat any wall or structure that defines the wells or well section of the microtiter plate as an inner wall. A structure that protrudes from the support and contacts any wall or structure of the well section of the microtiter plate will be treated as anticipatory of that feature of the claims. Relative to the software claim (claim 42), examiner notes that the placing step of claim 39 is written in a manner that it included manually placing the microtiter plate on the support. Thus this step is not being treated as limiting on the software claim along with the position that the microtiter plate is placed relative to the alignment members. Instant paragraph [00042] shows that the point of contact with the microtiter plate is preferably the inner wall but that it is not exclusively required to align the microtiter plate.
4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Art Unit: 1797

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-4, 7-8 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bevirt (US 6,063,579) in view of Kercso (US 6,132,685, newly cited and applied). In the patent Bevirt teaches an alignment mechanism to precisely position a work surface to facilitate the transfer of materials in an automated manner. In column 1, Bevirt teaches that a microtiter plate or other piece of laboratory equipment that is subject to multiple rounds of heating and cooling during a series of manipulations may become nonuniform in the flatness of its working surface causing the depth of individual wells to vary and resulting in problems with automated material transfer from the plate. The invention overcomes the described problem during material transfer processes by providing a method for flattening or elongating the work surface in order to precisely align the work surface in relationship with a dispenser. Figure 1 shows the positioning means (24,26) including structure on two perpendicular axes (see column 3, lines 1-14). In figures 4-5 the functioning of the device is taught. As illustrated in figure 4, a plate, such as a 384-well microtiter plate (50), is placed on a mold (52). The figure shows the positioning of the microtiter plate prior to applying pressure. The microtiter plate is shown elevated from the bottom surface (54) of the mold and supported by the top portion (56) of an elastomeric seal (58). An internal structure (60, alignment member in contact with an inner wall of the plate) is used to correctly position the microtiter plate with respect to the structure prior and during the application of a vacuum. The figure also shows a vacuum channel (62) leading from a vacuum port to individual vacuum outlets. Figure 5 illustrates how the plate is deformed to flatten the work surface of the assay plate once pressure is applied. The microtiter plate (70) has a plurality of wells (72), each having a well bottom (74), which may contact the bottom surface (76) of the mold. An internal structure (78, alignment member in contact with an inner wall of the plate) keeps the microtiter plate centrally positioned with respect to the rest of the mold and any material dispenser positioned above the mold structure. Once pressure is applied, the elastomeric seal (80) is sufficiently flexible to allow for vertical or horizontal motion of the outer rim (82) of the plate when the plate is compressed against the substantially planar upper surface

(84) of the mold. The position of the center region (86) is maintained by the internal structure. Typically, as a consequence of the movement of the plate, the shape of the elastomeric seal has changed. Bevirt does not teach placement of locating structures in contact with an edge of a well area of the microtiter plate.

In the patent Kercso teaches improved systems, devices, and methods for analyzing a large number of sample compounds contained in standard multiwell microtiter plates or other array structures. The multiwell plates (12) travel along a conveyor system to a test station having a microfluidic device. At the test station, each plate is removed from the conveyor and the wells of the multiwell plate are sequentially aligned with an input port of the microfluidic device. After at least a portion of each sample has been input into the microfluidic channel system, the plate is returned to the conveyor system. Pre and/or post testing stations may be disposed along the conveyor system, and the use of an X-Y-Z robotic arm and a plate support bracket (56) allows each of the samples in the wells to be input into the microfluidic network through a probe affixed to a microfluidic chip. The plate support structure for robotic manipulation of the plurality of assay samples is shown the various views of figures 3 and 6-8. It has a beam defining a proximal end and a distal end with an axis therebetween. An upwardly oriented tab (94) near the distal end of the beam inhibits axial movement of the plate when the plate rests on the support structure. The assay samples are disposed in wells of a plurality of plates, each plate (12) includes a plurality of wells (70) defined in an upper surface (72) of the plate. A lower surface (74) will typically define at least one recess disposed between the wells and a front edge (76), left and right edges (78,80) and a back edge (82). To fully constrain the plate when it rests on the bracket, the bracket takes advantage of the generally unused recess between the wells and the edges of the plate. The bracket includes a proximal mounting surface (90) and an elongate beam (92) extending distally to an upwardly oriented tab (94). Tab 94 limits axial movement of the plate, recess (75) optionally fittingly receiving the tab between wells and the front edge (see figures 7-8). Axial movement of the plate may further be inhibited by an end wall (96) adjacent the mounting surface. Column 13, lines 9-11 teach that the term "tab" encompasses a variety of structure shapes, including pins, posts, etc., that are upwardly oriented at the distal end of the beam. To laterally constrain the plate, the bracket further includes sidewalls (98) which fittingly receive the side edges of the plate therebetween.

Although the plate is shown with its longest dimension aligned parallel to beam 92, Kercso teaches that other orientations are also possible.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have placed alignment structures as taught by Kercso in the Bevirt device because of the advantages of utilizing the space between the wells and the outer wall as taught by Kercso and the ability to assist in the alignment of the plate.

6. Claims 1-13, 21-24, 27-28, 35 and 37-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burton (WO 99/04228) or Modlin (US 6,071,748) in view of Cathcart (US 5,443,791), Markin (US 5,417,922), Bevirt as explained above and Kercso as explained above. The published application and the Modlin patent have equivalent disclosures. Since both have equivalent disclosures the patent will be described. The anticipatory disclosure in the published application is shown in figures 40-43 and described on pages 46-51. In the patent Modlin describes a high-throughput light detection instrument. Figure 24 shows a general structure in which the light detection instrument is a part. Column 2 lines 56-62 discusses what is typical in current automated high-throughput analyzers including assay analyzers, liquid handling systems, robotics, computers for data management, reagents and assay kits, and microplates for automation of sample dispensing to data collection. In figures 22(a-c) and 23 Modlin teaches a transporter assembly used in the light detection device of the patent. Figures 22a-b show a stage for supporting a composition for analysis by the analyzer in the form of a transporter (600). The transporter includes a transporter body (602) and substantially parallel first and second transporter flanges (604a,b) that extend outward from the transporter body. First and second transporter flanges terminate in first and second transporter extensions (606a,b) that turn in toward one another without contacting one another. The transporter body, flanges, and extensions lie substantially in a plane and define a transporter cavity (608) that is larger than any sample containers that the transporter is intended to support. The shape of this cavity, rectangular, is chosen to accommodate the shape of the preferred sample containers, such as microplates. In the analyzer, long sides of the rectangular sample container are positioned against the flanges. Transporter shelves (610) along portions of the body, the flanges, and the extensions form a structure that supports the bottom of the sample container. Other support mechanisms, such as **pins or pegs**, also could be employed instead of or in addition to shelves.

The transporter also includes an automatic sample container positioning mechanism (620) for precisely and reproducibly positioning sample containers within the cavity along Y and X axes with positioning arms (622a,b) that contact the sample container to control its Y and X position, respectively. The Y-axis positioning arm (622a) lies substantially within a channel (624) in the body and includes a rod (626a) having the bent shape shown. A first end (628a) of the rod terminates near the cavity with a bumper tab (630a,632) for engaging a sample container. A second end (634a) of the rod terminates away from the cavity in an actuator tab (636a) for controlling movement of the arm. An Y-axis biasing spring (642a) is present. X-axis positioning arm (622b) also lies substantially within the channel (624) in the body and is similar to the Y-axis positioning arm, except that the first end segment (628b) terminates in a lever tab (630b) in the X-axis positioning arm rather than a bumper. The X-axis positioning arm is connected via the lever tab to an X-axis positioning lever (654) that lies along the transporter flange (604b). The X-axis positioning lever includes two functional lever projections (656,658) and is pivotally mounted about a lever pivot axis (659) on the transporter near the intersection of the body and the flange (604b). A first lever projection (656) is substantially perpendicular to the flange (604b) and abuts the lever tab on the X-axis positioning arm for actuating the positioning lever. A second lever projection (658) also is substantially perpendicular to the flange (604b) and includes an edge (660) for contacting a sample container. In use the transporter occupies a loading position substantially outside a housing for a person, robot, or mechanical stacker to place a sample container into the cavity so that the bottom of the sample container rests on the transporter shelves. Under the action of both positioning arms, the sample container is precisely and reproducibly positioned (registered) against a reference corner (672) within the cavity. The biasing springs (642a,b) can be chosen to have different strengths, so that the X-Y positioning action is performed less or more forcefully. As long as the microplate is placed in any position on the lower guide shelves, it can be adjusted into place by the automatic microplate positioning mechanism. A sensor (not shown) detects the presence of the sample container. The transporter can also eject the sample containers. Figure 23 shows a perspective view of the transporter mounted on base platform (700) with drive mechanisms for moving the transporter between loading and examination positions. The drive mechanism is provided multiple mechanisms for moving the transporter. Since the microtiter plate is not positively

recited as an element of the structure, where it is touched by the alignment member(s) has no patentable moment relative to the positively recited structure. The Burton application and Modlin patent do not teach specifics regarding the structure for liquid handling systems, robotics and reagent, assay kit and microplate storage.

In the patent Cathcart teaches an automated Molecular biology laboratory. In the device a liquid-handling instrument has a worksurface with registration for modular stations to support containers of liquid, pipette apparatus with a pipette tip coupled to a sensing circuit, a robotic translation system for moving the pipette tip, and a control system with an iconic user interface for programming and editing. A gauge block registered on the worksurface provides for calibration using the sensing tip, and register cavities on the worksurface provide for modular stations. There is a wash station for the pipette tip on the worksurface. An automated laboratory based on the liquid-handling system has heating and cooling and a sealable incubation station as well as a magnetic separation station. Methods are disclosed using the apparatus to convey droplets of liquid, to aspirate with minimum tip contamination, to mix liquids in containers, and to validate the worksurface. Procedures in chemistry, particularly in biochemistry, present generally more difficult problems for automation than many other kinds of processes and procedures. One reason is that there is often a very long sequence of steps in a biochemical procedure, such as gene detection and sequencing DNA. Another is that an automatic system needs to be very versatile, because different kinds of starting materials and different analytical purposes require different steps, different order of steps and the use of different kinds of chemical reagents. A third is that sample quantity is, for various reasons, quite limited, and only very small volumes, often on the order of microliters, must be used. What is needed is automatic robotic apparatus for doing liquid transfers with very small quantities of liquids, and in a manner that avoids carryover and evaporation. Such an instrument needs to be modular in nature so that container stations may be interchanged, with modular stations for holding containers so that such operations as sample preparation and cleaning may be done off-line. Methods for operation of such apparatus are needed allowing a relatively large number of samples to be processed at a time, with samples and reagents placed in a close array to preserve space. The robotic actions need to be rapid to minimize overall processing time and extremely accurate to be able to access many small sites. Such an apparatus needs to be integrated with a control system that allows an



operator to easily and quickly set up procedures with different variables, different step sequences, and different samples and reagents. Also needed is laboratory apparatus based on such a liquid handling system to incorporate further techniques, such as temperature control and a separation station, to be able to fully automate specific chemistry protocols such as for gene detection and DNA sample purification. The general form of the apparatus is shown in figure 1 and for performing DNA sequencing the automated laboratory has a closeable, heated, clamped-lid thermal cycling station (21), an actively cooled enzyme storage station (23), a wash station (25), a reagent storage position (27) for storing and presenting frequently used reagents, a DNA sample stage (28), a wash buffer storage (30), and two magnetic particle wash stations (26,29) for manipulating paramagnetic particles in suspension in liquid mixtures. Also shown is a gauge block (24) for use in calibrating the robotic drives for the apparatus. The various stations are arranged on a worksurface (22). In the preferred embodiment the stations on the worksurface are registered in cavities machined into the worksurface maintaining close tolerance dimensions from cavity to cavity and to the position of the gauge block, so modular stations may be interchanged while maintaining information about the position of containers relative to the worksurface and the gaugeblock.

In the patent Markin teaches a specimen carrier for transporting conventional specimen tubes throughout an automatic laboratory conveyance system includes a generally rectilinear carrier body with a forward face having an identification zone delimited thereon. An identification code is marked in the identification zone so as to permit mechanical sensing and identification of the carrier on a conveyor system. A plurality of holes of various diameters and depths are provided in the top surface of the carrier to receive conventional specimen tubes of various types with the top ends of the specimen tubes located at a predetermined height above the top surface of the carrier. A specimen carrier (10) may be temporarily stored on storage racks (70), as shown in figure 6. Each storage rack includes a base plate (72) with a plurality of locator pins (74) projecting upwardly from the upper surface of the base plate. Locator pins are arranged in sets of pairs that are longitudinally spaced apart so as to correspond with a pair of apertures (62,64, see figure 3) on each specimen carrier. Pin pairs are spaced apart laterally a distance such that specimen carriers are laterally spaced apart to permit the specimen carrier to be grasped by the jaws (76) of a robot arm (78).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the various components of Cathcart, Markin and Bevirt into the Burton or Modlin analyzers because of the ability to carry out complex procedures such as the high-throughput procedures of Burton or Modlin in a minimal amount of time as taught by Cathcart. It additionally would have been obvious to one of ordinary skill in the art at the time the invention was made to have placed the alignment members of Burton or Modlin so that they would contact an inner wall of the microtiter plate as shown by Kercso because of the positioning capabilities of placing alignment members as taught by Kercso.

7. Claims 14-15 and 17-20 are allowed.

8. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection. The Kercso reference has a clear teaching of advantages related to placing retaining/alignment members in the unused recess or space between the wells and the outer wall of a standard microtiter plate.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additionally cited art relates to vacuum manifolds to hold microtiter filtration plates and structures to hold microtiter plates for manipulating and handling.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (571)272-1265. The examiner can normally be reached on Monday-Thursday and Alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Arlen Soderquist/  
Primary Examiner, Art Unit 1797